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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/441,055	USUDA ET AL.	
	Examiner	Art Unit	
	Christian L Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-9 and 11-40* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 11-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Applicants' election traverse of Group III, claims 31-40, is acknowledged. The traversal is on the grounds that no reasons and/or examples are provided to support a conclusion of patentable distinctness and that a search of all the inventions would not be a serious burden. The Examiner disagrees for reasons of record as supplemented below.

Each of the methods of Groups I-III are distinct sine each method employs a different microorganism used in the production of L-methionine. A search of all the inventions in the patent literature and the non-patent literature cannot be made without serious burden because the inventions require separate searches that have different limits, boundaries, scope, and subject matter. The species requirement for claim 31 stated in the previous Office Action has been withdrawn.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their divergent subject matter, restriction for examination purposes is proper.

Claims 1-9, 11, and 12-30 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. The restriction requirement is still deemed proper and is therefore made FINAL.

2. Claims 31-40 are under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 31-40 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 31-40, as written, do not sufficiently distinguish over nucleic acids, proteins, cells or antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered

non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "transformed microorganism" or "recombinant microorganism". See MPEP 2105.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 31-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are genus claims that are directed toward any method for making L-methionine using any microorganism that is deficient in any repressor of any sequence/structure of any enzyme/protein involved in L-methionine biosynthesis and any homoserine transsuccinylase of any sequence/structure that is enhanced by any genetic modification. Claim 33 encompasses said microorganism further comprising a reduced intracellular activity of S-adenosylmethionine synthetase of any sequence/structure made by any genetic modification, has L-threonine auxotrophy, has enhanced intracellular activity of cystathionine gama-synthase of any sequence/structure and aspartokinase-homoserine dehydrogenase II of any sequence/structure made by any genetic modification.

However, the specification only describes a transformed E. coli strain which is deficient in expression of *metJ* encoding the E.coli repressor and contains an overexpressed *metA* encoding the E. coli homoserine transsuccinylase comprising SEQ ID NO: 26, SEQ ID NO: 26 where arginine is replaced with cysteine at position 27, SEQ ID NO: 26 where isoleucine is replaced with serine at position 296, or SEQ ID NO: 26 where proline is replaced with leucine at position 298. Furthermore, the specification only describes the metK, metB, and metL genes from E.coli.

The specification fails to provide a written description of additional representative microorganisms reciting the desired properties of deficiency in any repressor of any sequence/structure of any enzyme/protein involved in L-methionine biosynthesis and enhanced activity of any homoserine transsuccinylase of any sequence/structure made by any genetic

modification.

Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

7. Claims 31-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing L-methionine using a transformed E. coli strain which is deficient in expression of *metJ* encoding the E.coli repressor and contains an overexpressed *metA* encoding the E. coli homoserine transsuccinylase comprising SEQ ID NO: 26, SEQ ID NO: 26 where arginine is replaced with cysteine at position 27, SEQ ID NO: 26 where isoleucine is replaced with serine at position 296, or SEQ ID NO: 26 where proline is replaced with leucine at position 298; does not reasonably provide enablement for any other embodiment.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass any method for making L-methionine using any microorganism that is deficient in any repressor of any sequence/structure of any enzyme/protein involved in L-methionine biosynthesis and any homoserine transsuccinylase of any sequence/structure that is enhanced by any genetic modification.

The specification provides guidance and examples for [a transformed E. coli strain which is deficient in expression of *metJ* encoding the E.coli repressor and contains an overexpressed *metA* encoding the E. coli homoserine transsuccinylase comprising SEQ ID NO: 26, SEQ ID NO: 26 where arginine is replaced with cysteine at position 27, SEQ ID NO: 26 where isoleucine is replaced with serine at position 296, or SEQ ID NO: 26 where proline is replaced with leucine at position 298; and use of said transformed E. coli for the production of L-methionine].

However, the specification does not teach the specific identity and sequence/structure of any repressor of any enzyme or protein involved in L-methionine biosynthesis or the specific sequence/structure of any homoserine transsuccinylase that is enhanced by any genetic modification.

The standard for meeting the enablement requirement is whether one of skill in the art can make the invention without undue experimentation. The amount of experimentation to make the claimed invention is undue and outside the scope of routine experimentation since one must search for and identify any repressor of any enzyme or protein involved in L-methionine biosynthesis, the specific sequence/structure of any homoserine transsuccinylase and the specific

genetic modification resulting in increase enzyme activity, and determining whether any microorganism containing the desired properties is able be used in the claimed method for producing L-methionine. Furthermore, predictability in the art of success is extremely low since no information is provide by the specification regarding the specific identity and sequence/structure of any repressor of any enzyme or protein involved in L-methionine biosynthesis or the specific sequence/structure of any homoserine transsuccinylase that is enhanced by any genetic modification.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific identity and sequence/structure of any repressor and the specific sequence/structure of any homoserine transsuccinylase and the specific genetic modification resulting in an increase of enzyme activity . Without such a guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 37-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 37-39 recite the limitations "S-adenosylmethionine synthetase is encoded by the metK gene", "cystathionine synthase is encoded by the metB gene", and "aspartokinase homoserine dehydrogenase II is encoded by the metL gene", respectively. There is insufficient antecedent basis for the recited limitations in claims 37-39 which depend from claim 32.

Claims 37-39 should depend from claim 33 which recites the specific enzymes that are to be encoded by the genes recited in claims 37-39.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (571)272-0929. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571)272-0928. The offical fax phone number (703)872-9306. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (571)272-1600.

CLF

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